

REPORT DOCUMENTATION PAGE

AD-A212 435

DTIC FILE CO

DUE

DISTRIBUTION/AVAILABILITY

DISTRIBUTION/AVAILABILITY OF REPORT
Approved for public release; distribution is unlimited

5. MONITORING ORGANIZATION REPORT NUMBER(S)

7A. NAME OF MONITORING ORGANIZATION
Naval Medical Command7B. ADDRESS (City, State, and ZIP Code)
8901 Wisconsin Avenue
Bethesda, MD 20814-50558A. NAME OF FUNDING/SPONSORING
ORGANIZATION Naval Medical
Research & Development Command8B. OFFICE SYMBOL
(If applicable)

9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER

10. SOURCE OF FUNDING NUMBERS
PROGRAM ELEMENT NO. PROJECT NO. TASK NO. WORK UNIT
62233N MM33C30 004 1002
ACCESSION11. TITLE (Include Security Classification)
Propranolol accentuates the cold induced fall in skin temperature and elevation in blood
pressure in 12 normotensive men: a role for the beta receptor in cold

12. PERSONAL AUTHOR(S)

HL Reed, KR Kowalski, MM D'Alesandro, R Robertson, and SB Lewis

13a. TYPE OF REPORT

13b. TIME COVERED

FROM 1986 TO 1988

14. DATE OF REPORT (Year, Month, Day)

1989 March 20

15. PAGE COUNT

10

16. SUPPLEMENTARY NOTATION

This poster was presented at the Annual FASEB Meeting in New Orleans, LA, March 19-23 1989.

17. COSATI CODES

18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)

FIELD GROUP SUB-GROUP

Hypertension, Norepinephrine, Epinephrine

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

Exposure to cold air induces a rapid and characteristic rise in plasma norepinephrine

and blood pressure. The mechanism of this cold induced hypertension, which is independent

of renin, appears to be mediated by adrenergic receptors. To test this hypothesis, we

administered propranolol (80mg/day: 1mg/kg), a beta adrenoreceptor blocker, and contrasted

this response with the sympathomimetic drug ephedrine (60 mg/day: .9 mg/kg) and placebo.

We used a double blind cross over study. Twelve normotensive men entered a climatic chamber

for a 30 minute exposure of either 4°C or 25°C. Fingertip capillary blood flow was estimated

by a laser doppler technique, while fingertip skin and rectal temperatures were recorded.

We serially measured brachial blood pressure/pulse and hematocrit. As indicators of sym-

pathetic nervous system activity, venous plasma norepinephrine (NE) and epinephrine (EPI)

were measured.

Cold exposure induced a rapid decrease in skin capillary blood flow from 117 +/- 38 mv

44 +/- 10 mv within one minute of entering a 4°C cold room. This decrease was associated

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT

21. ABSTRACT SECURITY CLASSIFICATION

UNCLASSIFIED/UNLIMITED SAME AS RPT DTC USERS Unclassified

22a. NAME OF RESPONSIBLE INDIVIDUAL

22b. TELEPHONE (Include Area Code)

(202) 295-0198

22c. OFFICE SYMBOL

SD/RSD/NMRI

DD FORM 1473, 84 MAR

83 APR edition may be used until exhausted

All other editions are obsolete

SECURITY CLASSIFICATION OF THIS PAGE

UNCLASSIFIED

10 186

TABLE OF CONTENTS

	<u>Page No.</u>
Introduction	1
Methods	1
Results	2
Conclusion	2
Acknowledgments	3
Figure Legends	4

LIST OF FIGURES

Figure 1	6
Figure 2	7
Figure 3	8
Figure 4	9
Figure 5	10



Accession For	
NTIS GRA&I <input checked="" type="checkbox"/>	
DTIC TAB <input type="checkbox"/>	
Unannounced <input type="checkbox"/>	
Justification	
By	
Distribution/	
Availability Codes	
Dist	Avail and/or
	Special
A-1	

INTRODUCTION

- " The mechanism of cold induced non-renin hypertension is unknown but is likely mediated by norepinephrine.
- " We have isolated the β -receptor effects of the cold associated elevations in norepinephrine by blocking these receptors with propranolol.
- " This blockade is contrasted during cold exposure with the treatment of ephedrine, an agent known to increase peripheral vascular resistance and blood pressure.

METHODS

- " Twelve healthy males age 27.9 ± 1.9 years
- " Thermal air tests: control: 25° C; 30 minutes
cold: 4° C; 30 minutes
- " Drugs: ephedrine (.9 mg/kg)
propranolol (1 mg/kg)
placebo
- " Protocol: post-absorptive
seminude
motionless
- " Blood pressure
- " Capillary blood flow
- " Skin (finger) temperature
- " Plasma catecholamines
- " Curve fitting determination of the rate of change of temperature and blood flow.

RESULTS

- " Propranolol accentuates the cold induced rise in blood pressure compared to placebo and ephedrine.
- " Capillary blood flow rapidly declines with a cold air exposure and precedes the fall in skin temperature.
- " Propranolol administration is associated with lower finger temperatures during a cold air exposure.
- " Plasma norepinephrine values are not different between propranolol and placebo treatments.

CONCLUSION

- " Beta adrenergic receptor attenuates the physiologic response to cold.

ACKNOWLEDGMENTS

Research and Development Command work unit number 62233N.MM33C30 004.1002. The opinions and assertions expressed herein are the private ones of the authors and are not to be construed as official or reflecting the views of the Department of Defense, the Department of Navy, or the Naval Service at Large.

FIGURE LEGENDS

1. The average \pm SE mean arterial pressure (MAP) measured in 12 men before, during and after a thirty minute exposure to either control (25° C) or cold (4° C) air. All were acutely pretreated with propranolol (1.0mg/kg/day), ephedrine (0.8mg/kg/day) or placebo, and tested at each temperature, the last dose of the agent ingested 30 minutes before entering the chamber. Time is minutes after entering the chamber (0 min). Five minutes after entering the chamber (35 minutes after ingestion of the agent) the MAP between the drug treatment groups studied at 25° C became different and remained so for the duration of the exposure. Difference between drug and placebo at 25° C ($p<0.05$) measured by a two way ANOVA.
2. Fingertip capillary blood flow, determined by placing the probe of a laser doppler velocimetric recorder on the distal pad of the index finger, declines within one minute of exposure to cold air. Fingertip skin temperature of the middle finger drops gradually. These data were used to fit a single exponent model which provided smoothed estimates of temperature and blood flow values.
3. Fingertip Blood flow is expressed as the mean \pm SE mv of the 12 subjects. Blood flow is recorded before, during, and after the thirty minute exposure to either control (25° C) or cold (4° C) air, with pretreatment of either placebo, ephedrine or propranolol. Time is in minutes, similar to Figure 1. The fingertip blood flow drops within one minute in the cold air exposures, remaining depressed for the thirty minute period.
4. Fingertip temperature, is fit to a single exponent model and shown for

time points just before entering the chamber and after 30 minutes in the cold room. Bars represent the mean \pm SE fingertip temperature of the 12 men after pretreatment with placebo, ephedrine (0.8mg/kg/day), and propranolol (1.0mg/kg/day). Propranolol treatment results in a lower finger temperature after exposure to cold compared to placebo. Analysis is by two way ANOVA.

5. The mean \pm SE plasma norepinephrine (NE) and epinephrine (EPI) are measured in 12 men before during and after a 30 minute control (25° C) or cold (4° C) air exposure with pretreatment with placebo, ephedrine, and propranolol. NE values after pretreatment with ephedrine were significantly lower during the cold air exposure compared to placebo ($p<0.05$). Neither NE or EPI values were changed by the control temperature nor was there any difference between drugs and placebo in this setting. Analysis is by two way ANOVA. [Plasma NE and EPI may be converted to pg/ml by $NE(\text{nmol/L}) = NE(\text{pg/ml}) \times 0.005911$; $EPI(\text{pmol/L}) = EPI(\text{pg/ml}) \times 5.458$].

MEAN ARTERIAL PRESSURE WITH 4 DEGREE C AIR EXPOSURE

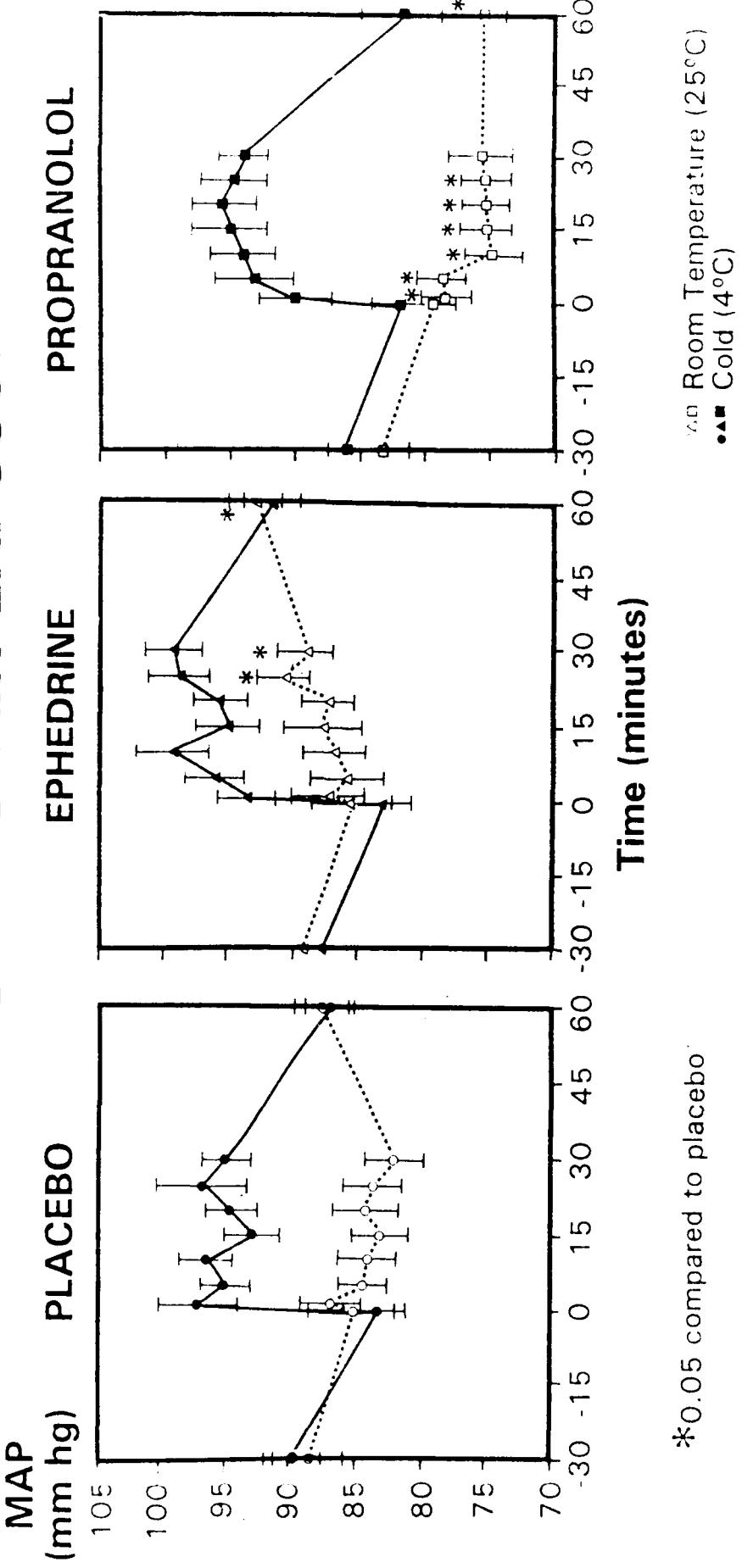
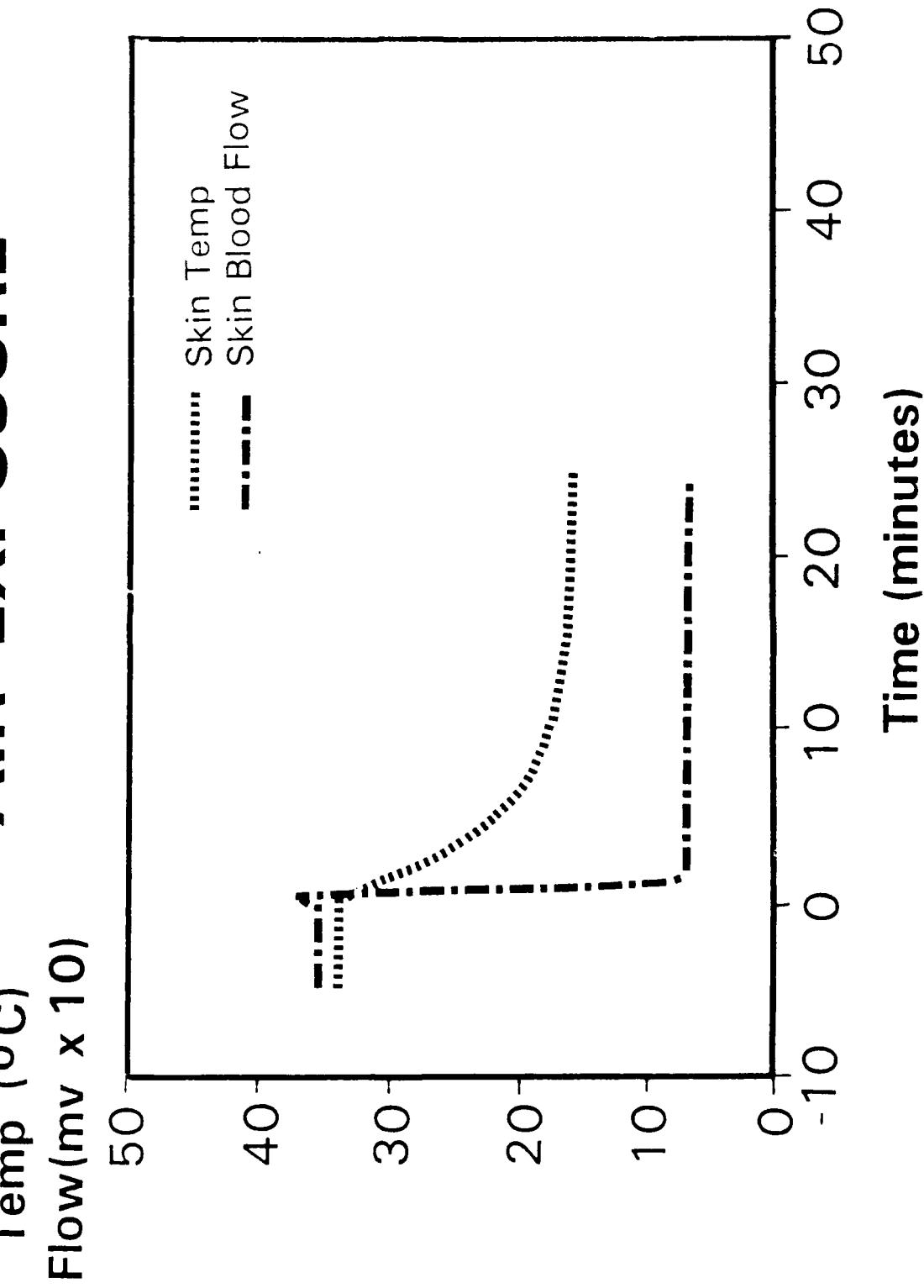
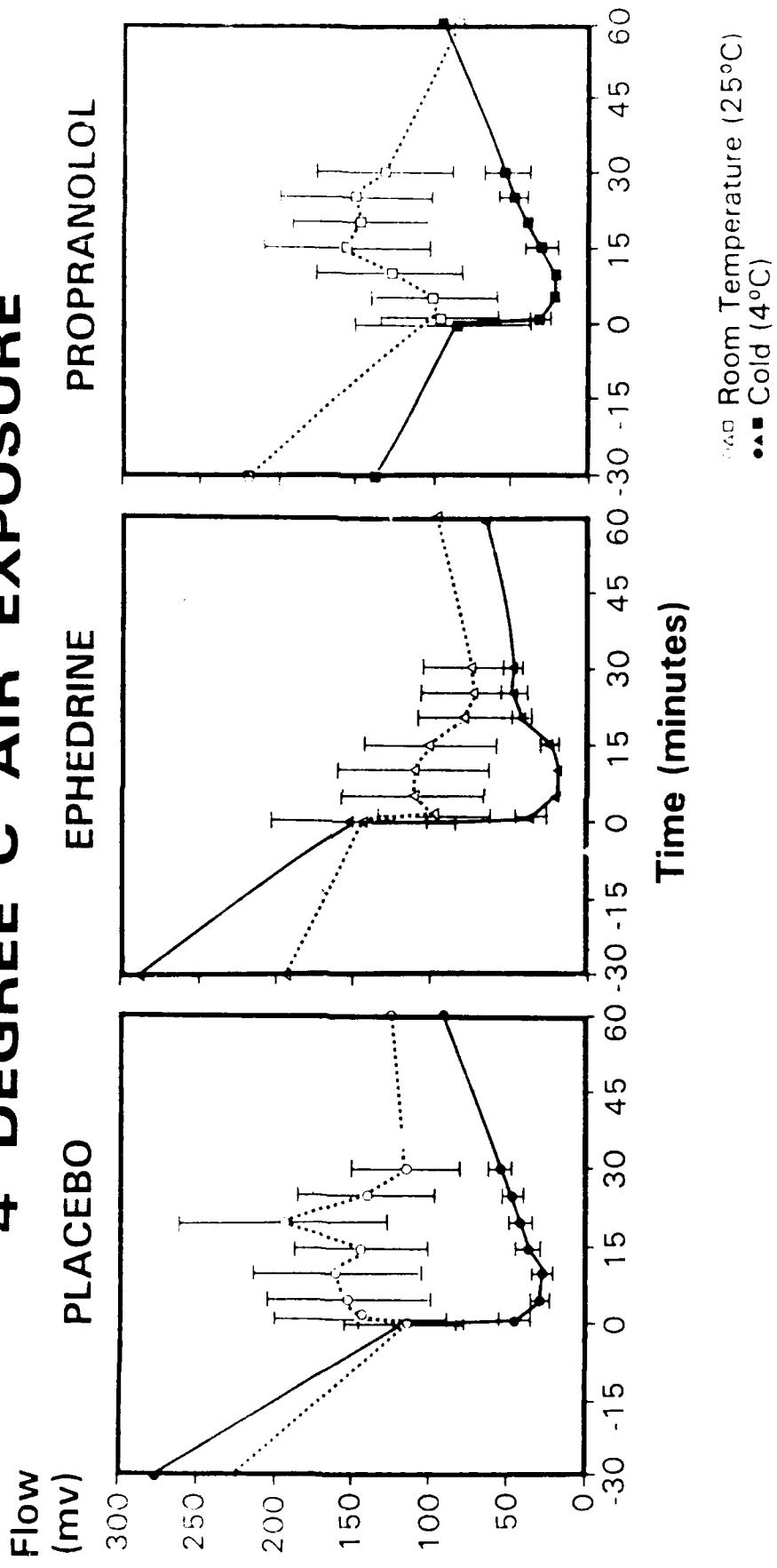


FIGURE 2

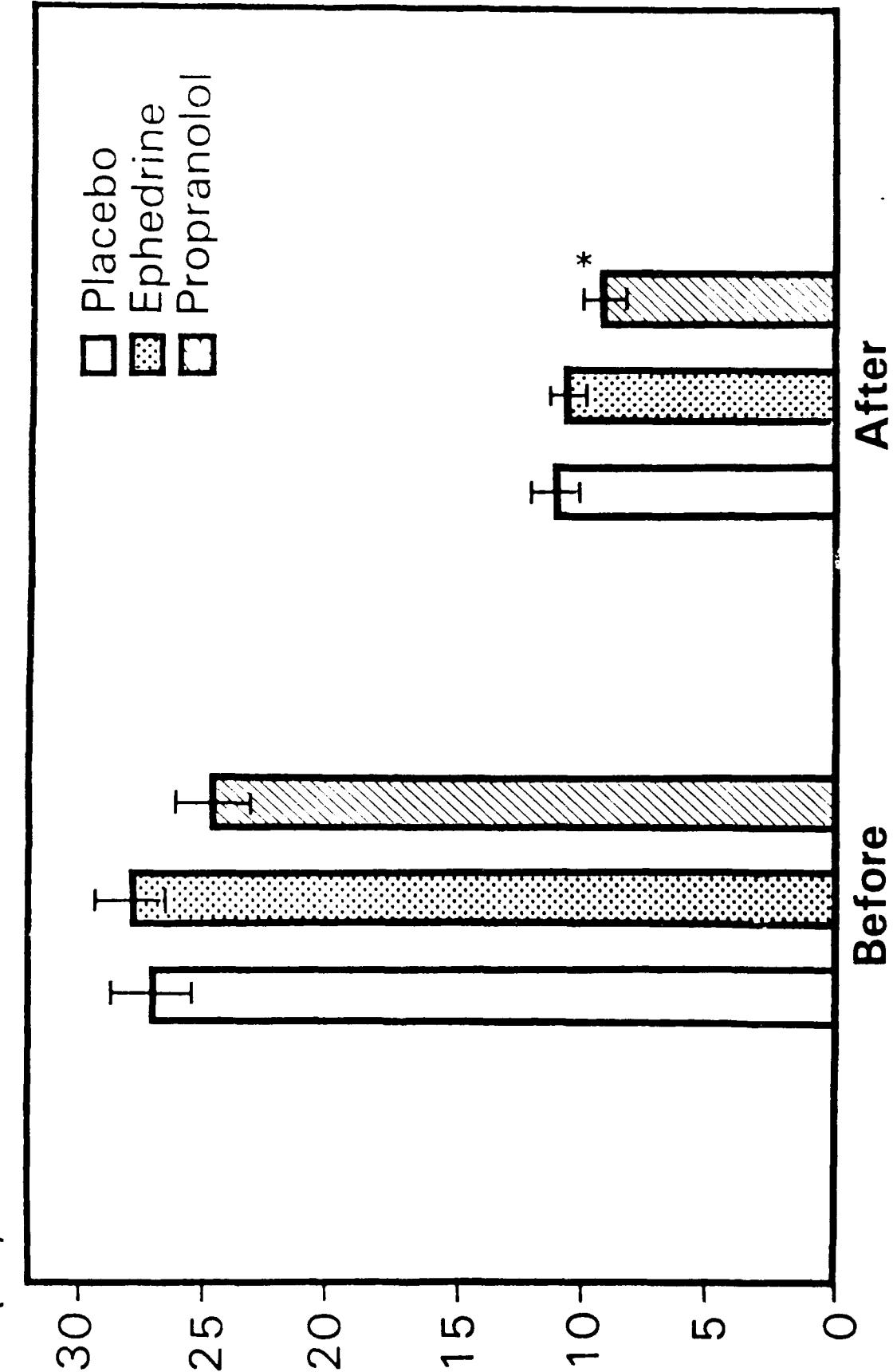
FINGER TEMPERATURE AND BLOOD FLOW WITH 4 DEGREE C AIR EXPOSURE



FINGERTIP BLOODFLOW WITH 4 DEGREE C AIR EXPOSURE



FINGER TEMPERATURE WITH 4 DEGREE C AIR EXPOSURE

Temp
(°C)



1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

26

27

28

29

30

31

32

33

34

35

36

37

38

39

40

41

42